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Molecular farming of recombinant antibodies in plants.

Schillberg S, Fischer R, Emans N.

Fraunhofer Institute for Molecular Biology and Applied Ecology, IME, Graftschaft, Auf dem Aberg 1, 57392 Schmallenberg, Germany.

Antibodies represent a large proportion of therapeutic drugs currently in development. In most cases, they are produced in mammalian cell lines or transgenic animals because these have been shown to fold and assemble the proteins correctly and generate authentic glycosylation patterns. However, such expression systems are expensive, difficult to scale up and there are safety concerns due to potential contamination with pathogenic organisms or oncogenic DNA sequences. Plants represent an inexpensive, efficient and safe alternative for the production of recombinant antibodies. Research over the last 10 years has shown that plants can produce a variety of functional antibodies and there is now intense interest in scaling up production to commercial levels. In this review, we discuss the advantages of plants over traditional expression systems, describe how antibody expression in plants is achieved and optimized and then consider the practical issues concerning large-scale molecular farming in plants. The first plant-produced therapeutic antibodies are already in clinical trials, and, given the economic benefits of this production system, we are likely to see many more recombinant antibodies produced in this manner in the future.

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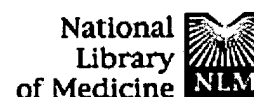
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FULL-TEXT ARTICLE**

Expression of a human, neutralizing monoclonal antibody specific to puumala virus G2-protein in stably-transformed insect cells.

Guttieri MC, Bookwalter C, Schmaljohn C.

Virology Division, United States Army Medical Research Institute of Infectious Diseases, Bldg. 1301, Fort Detrick, Frederick, MD 21702-5011, USA. mary.guttieri@det.amedd.army.mil

We cloned the heavy- and light-chain antibody genes of a human X (humanxmou) trioma secreting a neutralizing, IgG monoclonal antibody to the G2-protein of Puumala virus. The antibody genes were inserted separately into plasmid transfer vector pIEI-4 such that the genes were under control of the baculovirus immediate early gene promoter, IEI. *Trichoplusia ni* (TN) cells were co-transfected with these constructs and a selection plasmid containing a neomycin-resistance gene. Cloned transformants expressing the IgG monoclonal antibody were identified by ELISA of transfected TN cell culture supernatants. TN cell lines were established from four selected clones, of which one was chosen for detailed analysis. Specificity of the insect cell-expressed human antibody was determined by ELISA with Puumala virus-infected cell lysates and by immune-precipitation of radiolabeled Puumala virus proteins. The expressed IgG retained the ability to neutralize Puumala virus in plaque-reduction neutralization assays. Using competitive polymerase chain reaction methods, multiple copies of integrated heavy- and light-chain antibody genes were detected in the insect cell genome. The transformed insect cells were stable and continuously expressed biologically active IgG. We conclude that this methodology provides an alternative eukaryotic source for the generation of human antibodies.

PMID: 11121551 [PubMed - indexed for MEDLINE]

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